

COMPUTER MODELLING AND EXPERIMENTAL VALIDATION OF SMOOTH MUSCLE CELL GROWTH USING MATRIGEL AS A BASEMENT MEMBRANE MATRIX

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OVERVIEW: In the assessment of activities which lead toward functional tissue engineering of arterial replacements, it is evident that a need exists for a support scaffold that is compliant and capable of nominal stretching and recovery. It should have lateral and transverse mechanical properties which would entertain the *in vivo* functionality of an artery under pulsatile flow in a range of internal pressure. Such scaffolds or matrixes are generally limited to polymers or porcine based cross-linked collagen. However, the prior mechanical and developmental history of the collagen and its associated tenacious structure resists ingress of the human smooth muscle cells delaying satisfactory growth and substitution of human collagen. This appears mainly to be due to the dense, aligned, matted structure, slow cell activity, and inadequate digestion of cross-linked porcine collagen.

In parallel work, the mechanical properties of cartilage replacements are being assessed using a gelatinous material (alginate), as a soft matrix support for chondrocyte cells to help them establish growth. In progression from this activity a computer model has been developed¹ and extended, which simulates the growth of human smooth muscle cells in such a gelatinous material but incorporating a surrounding connective tissue of a porcine collagen scaffold. The overall aim has been to simulate growth of an end product that includes a coating of endothelial cells to promote signalling and produce a non-thrombogenic surface. Therefore, another gel form, namely Matrigel, becomes a base for bonding agents or for direct seeding of mature endothelial cells. The computer modelling of the layers in this case was accomplished with a bespoke system using the finite volume method.

This paper reports on both the experimental validation, the methodology of the computational element and output of the simulation.

This has provided the basis for future work and provides basic data for a computer study of the mechanical properties of the Matrigel which may

confer improved elasticity and resistance to pressure fluctuations of the type experienced in lower arteries. Overall it is considered that this may provide a suitable growth environment for slow growing smooth muscle cells permitting time for their division and excretion of collagen. In this way, their growth and mobility will be relatively unhindered by the cross-linked porcine collagen.

CONCLUSIONS: This work combines a range of advances in cell culture and computer modeling, providing a rapid growth potential of active cells whilst providing a suitable environment for slow growing smooth muscle cells protected by a clinically acceptable outer sheath of pre-formed collagen or polymer.

Anticipated platforms and focus groups for further research created by this experiment include optimisation of assembly of the gel-based core, development of such matrices for clinical use, procedures and optimisation of pre-preparation of cells, and assessment of functionality prior to transplant.

The model provides a basis for the assessment of the finite volume method and its applicability to computational biology and tissue engineered products.

REFERENCES: ¹ Kirk, C.S., and Mileham, A.R., (2001), Modelling Diffusion in Heterogeneous Transition Welds using the Finite Volume Method, EPSRC Research Report and Assessment, University of Bath, 2001.